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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/423,554 | 11/10/1999 | ARISTOS ARISTIDOU | 0933-148P | 6884 |

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EXAMINER

WALICKA, MALGORZATA A

| ART UNIT | PAPER NUMBER |
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1652

DATE MAILED: 07/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | | |
|------------------------------|------------------------|--|---------------------|--|
| Office Action Summary | Application No. | | Applicant(s) | |
| | 09/423,554 | | ARISTIDOU ET AL. | |
| | Examiner | | Art Unit | |
| | Malgorzata A. Walicka | | 1652 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 02 May 2002.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-10, 17-22, 25, 26, 28-30, 33 and 38 - 39 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) 25 and 26 is/are allowed.

6) ☒ Claim(s) 1-10, 17-22, 28-30, 33 and 38 - 39 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some * c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

| | |
|---|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6) <input type="checkbox"/> Other: _____ |
|---|--|

The Reply under 37 CFR § 1.111, filed on May 2, 2002 as paper No. 14, is acknowledged. Claims 1-10, 17-22, 25, 26, 28-30, 33, 38 and 39 are pending in the application and are the subject of this Office Action.

Detailed Office Action

Response to the enquiry regarding claim 39

Claim 39 was included in the rejection in the previous Office Action, paper no. 13, under 35 USC, section 112, second paragraph, for the indefinite term "or causes the expression". Claim 39 was inadvertently missed from the enumeration of the rejected claims in the Office Action, but, as Applicants noted, was included in rejected claims in the Office Action Summary.

1. Objections

1.1. Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code see page 47, line 7 and 30. Applicant is *not corrected* required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The Specification is also objected because it misses a list of transformed *not entered* organisms, genes which are contained in plasmid, or integrated into the genome of an organism and the source/sequence identification numbers of the genes.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is requested in correcting any errors of which applicant may become aware.

1.2. Drawings

This application has been filed with informal drawings, which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

2. Rejections

2.1. 35 USC 112, second paragraph

Claim 1-10, 17- 22, 28-30, 33 and 38 and 39 are rejected under 35 U.S.C. 112, for the reasons indicate in the previous Office Actions, papers No. 10 and 13.

Claim 1

The term "functional coupling" in the phrase "functional coupling of the oxidation and reduction" of claim 1 is unclear. It seems that in a living cells the oxidation and reduction processes are coupled. The Applicants write on page 9, line 31: "the present invention provides a microorganism which is transformed with at least one recombinant DNA molecule encoding or otherwise causing the expression of at least one of the pair of dehydrogenases with opposite coenzyme specificities for NAD/NADH and NADP/NADPH, but at least one common substrate." It is unclear whether by "functional

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can be fixed by deleting functional coupling
coupling Applicants mean "expression of at least one of the pair of dehydrogenases with opposite coenzyme specificities for NAD/NADH and NADP/NADPH". If a cell expresses an endogenous dehydrogenase using NADP, transforming said cell with one exogenous dehydrogenase that uses NAD will cause the coupling. Otherwise, one has to transform the cell with a pair of dehydrogenases, one of which that uses NAD, the other NADP.

Furthermore, while Applicants may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "pyridine nucleotide" in claim 1 is used by the claim to mean "nicotinamide adenine dinucleotide or nicotinamide adenine dinucleotide phosphate", both in oxidized and reduced forms, while the accepted meaning is "pyridine nucleotide", i.e. a compound that consists of pyridine ribose and phosphate.

Besides, the terms "more efficiently" and "more reduced" in claim 1 are relative terms which render the claim indefinite. The term "more efficiently" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Dependent claims 2-10, 18-20, 22, 28-30, 33 and 38 are including into rejection because they do not correct deficiency of the claim from which they depend.

Claim 3

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The term "producing a product faster" in claim 3 is a relative term, which renders the claim indefinite. The term "faster" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 4

The term "less CO₂" in claim 4 is a relative term, which renders the claim indefinite. The term "less" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 5

The phrase "reduced oxygen requirement per unit of a product produced" is indefinite and renders the claim indefinite. Neither the claim nor the specification provides a definition of the term "oxygen requirement". In addition, the term "reduced oxygen requirement" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 6 and 7

Claim 6 and dependent claim 7 are rejected because the meaning of the phrase "conditions of a biotechnological process" 6 is not clear to one skilled in the art. He or she would not know what makes a process "biotechnological".

2.2. 35 USC 112, first paragraph

New rejection under 35 USC 112, first paragraph

Lack of written description

Claims 1-10, 17- 22, 28-30, 33, 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

*express
of particular gene
was
not
shown* The claims are directed to a microorganism transformed with at least one recombinant DNA molecule causing the expression of a gene of at least one enzyme that causes the coupling the oxidation and reduction of substrates by two dehydrogenase reactions. The claims are directed to the large genus of microorganisms transformed with any of DNA molecule such as promoters, enhancers, or transcription factors for many genes, from any natural source, as well as artificial. The disclosure fails to teach such microorganism and such DNA molecules. Applicants only mention, without identifying nucleotide sequences, promoters such as PGK or ADH causing expression of constitute NAD-dependent glutamate dehydrogenase in *S. cerevisiae* (page 26, line 11). However, Applicant do not disclose any *S. cerevisiae*

transformant comprising said promoters nor guide how to perform *in vivo* recombination so that these promoters were incorporated in the proper place of the *S. cerevisiae* genome. Furthermore, those skilled in the art are aware that promoters suitable for glutamate dehydrogenase in *S. cerevisiae* are not suitable for other genes encoding enzymes useful in making the claimed invention, as well as for other microorganisms to be transformed. Thus, because Applicant do not teach any microorganism that has expression of a gene of interest enhanced by any of the large species of the above-enumerated DNA molecules, the one skilled in the art is not convinced that the inventors, at the time the application was filled, had possession of the claimed invention.

Lack of enablement

Claim 1-10, 17- 22, 28-30, 33, 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a microorganism transformed with at least one recombinant DNA molecule causing the expression of a gene of at least one enzyme that causes the coupling of oxidation and reduction of substrates by two dehydrogenase reactions. However, to make such transformed microorganism one has to know promoter sequences of the genes of interest and replace them by homologous recombination. Alternatively, one has to know the enhancer or transcription factor sequences acting on DNA encoding the enzyme of interest and a guidance how to

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perform the homologous recombination to obtain the claimed transformant. Without further guidance on the part of Applicants how to make said transformants claimed invention necessitates undue experimentation.

Factors to be considered in determining whether undue experimentation is required, are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any microorganism transformed with DNA molecules from any organism or man-made that increases expression of a gene of at least one enzyme that causes the coupling the oxidation and reduction of substrates by two dehydrogenase reactions. Although the art of causing or increasing gene expression by transforming microorganism is pretty developed, and skills of those in the art high, the predicatability of the results is low. In addition, Applicants fail to give examples of transformation with DNA molecules that cause expression of at least one enzyme that causes the coupling the oxidation and reduction of substrates by two dehydrogenase reactions in any microorganism. Thus, Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims.

Without further guidance on the part of applicants as to which DNA molecule to use for induction or increase in expression of particular gene in particular microorganism, results are unpredictable and probability of success very low. Thus without the further guidance, the experimentation left to those skilled in the art is improperly undue.

Conclusions


Claims 25 and 26 are allowed for reasons stated in the previous Office Action, paper No.10.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.
Art Unit 1652
Patent examiner


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PRIMARY EXAMINER